IN THE CLAIMS:

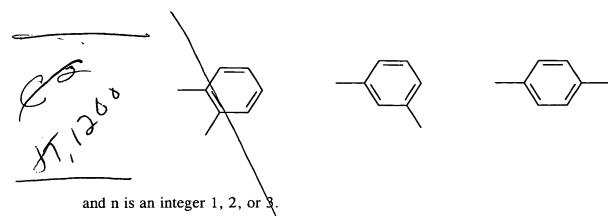
Kindly cancel claims 1, 14, 16 and 29-37 without prejudice or disclaimer.

Kindly replace claims 2-13, 15, 17-28 and 38-41 as follows.

- 2. (Thrice Amended) The method according to claim $\frac{3}{8}$ wherein R_1 and R_2 are a hydrogen atom, a methyl group, or a methoxy group.
- 3. (Thrice Amended) The method according to claim 38 wherein R_3 is a hydrogen atom or a methyl group.
 - 4. (Thrice Amended) The method according to claim 38 wherein Z is

and n is an integer 0.

5. (Thrice Amended) The method according to claim 38 wherein Z is



- 6. (Thrice Amended) The method according to claim 38 wherein R_4 is a group $-COOR_5$ wherein R_5 is a hydrogen atom, an optionally substituted alkyl group having 1 to 8 carbons, an optionally substituted phenyl group, or an optionally substituted aralkyl group having 7 to 11 carbons.
- 7. (Thrice Amended) The method according to claim 38 wherein R_4 is a group $-\text{CONR}_6R_7$ wherein R_6 and R_7 are each independently a hydrogen atom, an optionally substituted alkyl group having 1 to 8 carbons, an optionally substituted bicyclic unsaturated or partially saturated hydrocarbon ring group having 9 to 11 carbons, an optionally substituted heterocyclic group, an optionally substituted phenyl group, an optionally substituted aralkyl group having 7 to 11 carbons, or a heteroaryl- C_1 - C_3 -alkyl group, or R_6 and R_7 , together with the nitrogen atom to which they are attached, represent a heterocyclic group which may further contain a nitrogen, oxygen, and/or sulfur atom.
- 8. (Thrice Amended) The method according to claim 38 wherein R_4 is a group $-\text{CONR}_6R_7$ wherein R_6 and R_7 , together with the nitrogen atom to which they are attached,

ر ا ا represent a 5- to 10-membered optionally substituted, nitrogen-containing heterocyclic group which may contain, in addition to the carbon and nitrogen atom, 1 to 3 heteroatoms selected from the group consisting of a nitrogen, oxygen and sulfur atom, the carbon atom on said cyclic group being optionally a ketone form or the sulfur atom on said cyclic group being optionally an oxide form.

9. (Thrice Amended) The method according to claim $\frac{2}{8}$ wherein R_1 and R_2 are a methyl group or a methoxy group; R_3 is a methyl group: R_4 is a carboxyl group which is optionally esterified or amidated; Z is

and n is an integer 1, 2, or 3.

10. (Thrice Amended) The method according to claim 38 wherein the suppressing agent for the gene expression of one or more substances is selected from the group consisting of IL-1, TNF-α, IL-2, IL-6, IL-8, iNOS, granulocyte colony-stimulating factor, inteferon-β, ICAM-1, VCAM-1, ELAM-1, major histocompatibility system class I, major histocompatibility system class II, β2-microglobulin, immunoglobulin light chain, serum amyloid A, angiotensinogen, complement B, complement C4, c-myc, HIV, HTLV-1, SV40, CMV, and adenovirus.

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11. (Thrice Amended) The method according to claim 38 which is a prophylactic or treatment for inflammatory diseases.

- 12. (Thrice Amended) The method according to claim 38 which is a prophylactic or treatment for autoimmune diseases.
- 13. (Twice Amended) The method according to claim 38 which is a prophylactic or treatment for viral diseases.

(3

(Amended) The method according to claim 38 wherein the compound is selected from:

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]morpholine,

N-[3-(4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]thiomorpholine\S-oxide,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4 benzoquinon-2-ylmethyl)phenyl]propionyl]thiomorpholine S-dioxide,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]piperidine,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]dimethylamine,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phanyl]propionyl]isopropylamine,

N-(3-(4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]ethanolamine,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]benzylamine,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]phenethylamine,

N-[3-(4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]acryloyl]morpholine,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]acryloyl]thiomorpholine,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]acryloyl]piperidine,

N-[3-(4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]acryloyl]dimethylamine,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]acryloyl]isopropylamine,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]acryloyl]ethanolamine,

N-[3-[4-(5,6-,dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]acryloyl]benzylamine,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]acryloyl]phenethylamine,

N-[3-[3-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]piperidine,

N-[3-[3-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]pronionyl]thiomorpholine,

N-[3-[3-(5,6-di-methoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]morpholine,

N-[3-[3-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]isopropylamine,

3-[3-(5,6-dimethoxy-3-methyl-\,4-benzoquinon-2-ylmethyl)phenyl]acrylic acid,

N-[3-[3-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]acryloyl]piperidine,

N-[3-[3-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]acryloyl]morpholine,

N-[3-[3-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]acryloyl]isopropylamine,

N-[3-[3-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]acryloyl]thiomorpholine,

N-[3-[4-(3,5,6-trimethyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]isopropylamine,

N-[3-[4-(3,5,6-trimethyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]piperidine,

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N-[3-(4-(3,5,6-trimethyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]morpholine,

N-[3-[3-(3,\5,6-trimethyl-1,4-benzoquinon-2-

ylmethyl)phenyl]propionyl]isopropylamine,

N-[3-[3-(3,5,6-\frimethyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]piperidine,

3-[2-(5,6-dimethoxy-3-methyl-1,4-benzoquino-n-2-ylmethyl)phenyl]acrylic acid,

N-[3-[2-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-

ylmethyl)phenyl]acryloyl]thiomorpholine,

3-[2-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionic acid,

N-[3-[2-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-

ylmethyl)phenyl]propionyl]piperidine,

N-[3-[2-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-

ylmethyl)phenyl]propionyl]morpholine,

N-[3-[2-(5,6-dimethoxy-3-methyl-1]]4-benzoquinon-2-

ylmethyl)phenyl]propionyl]thiomorpholine,

N-[3-[2-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-

ylmethyl)phenyl]propionyl]isopropylamihe,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]-

(s)-2-(methoxymethyl)pyrrolidine,

N-[3-(4-(5,6-dimethoxy-3-methyl-1,4-benzoquipon-2-

ylmethyl)phenyl]propionyl]isonipecotamide,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon\2-ylmethyl)phenyl]propionyl]-4-

methylpiperidine,

N-[3-[4-(5)6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]-2-methylpiperidine,

N-[3-[4-(5,6-d\methoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]-3-methylpiperidine,

N-[3-(4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]-4-methoxyaniline,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]-2-hydroxyaniline,

N-(3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]-3,4-dimethoxyaniline,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]-D,L-alaninol,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]-D,L-pipecolic acid ethylester,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4/benzoquinon-2-ylmethyl)phenyl]propionyl]-L-prolinamide,

4-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoqui non-2-ylmethyl)phenyl]propionyl] aminophenylacetonitrile,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]-4-pentylaniline,

N-[3-(4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl](s)-(-)-l-phenylethylamine,

126

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]-(R)-(+)-l-phenylethylamine,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]-1,3-dimethylbutylamine,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]cycloheptylamine,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]-3,5-dimethylpiperidine,

1-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]-4-ethoxycarbonylpiperazine,

1-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]-4-phenylpiperazine,

1-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]-4-hydroxy-4-phenylpiperidine,

1-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]-4(4-chlorophenyl)-4-hydroxypiperidine,

1-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2\vinethyl)phenyl]propionyl]-4-(2-methoxyphenyl)piperazine,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline,

4-acetyl-4-phenyl-1-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]piperidine,

27

N-(3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]-1,2,3,4-tetrahydroisoquinoline,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl] soamylamine,

N-[3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]cyclonexylamine,

N-(3-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]propionyl]-4-hydroxyaniline,

4-(5,6-dimethoxy-3-methyl-1,4-banzoquinon-2-ylmethyl)benzoic acid,

N-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)benzoyl]morpholine,

N-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-

ylmethyl)benzoyl]isopropylamine,

N-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)benzoyl]piperidine,

N-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-

ylmethyl)benzoyl]thiomorpholine,

3-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)benzoic acid,

N-[3-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-

ylmethyl) benzoyl] is opropylamine,

N-[3-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-xlmethyl)piperidine,

N-[3-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethxl)morpholine,

N-[3-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)thiomorpholine,

4-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]-n-butyric acid,



N-[4-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]butanoyl]morpholine,

N-[4-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]butanoyl]thiomorpholine,

N-[4-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]butanoyl]piperidine,

N-(4-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]butanoyl]isopropylamine,

4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenylacetic acid,

N-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenylacetyl]morpholine,

N-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenylacetyl]piperidine,

N-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenylacetyl]thiomorpholine,

N-[4-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenylacetyl]isopropylamine,

3-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenylacetic acid,

N-[3-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenylacetyl]piperidine,

N-[3-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-

ylmethyl)phenylacetyl]thiomorpholine,

N-[3-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenylacetyl]morpholine,

N-[3\(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenylacetyl]morpholine,

4-(3-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]-n-butyric acid,

N-[4-[3-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-

ylmethyl)phenyl]butanoyl]piperidine,

N-(4-[3-(5,6-dimetho--y-3-methyl-1,4-benzoquin on-2-

ylmethyl)phenyl]butanoyl]thiomorpholine,

N-[4-[3-(5,6-dimethoxy-3-methy]],4-benzoquinon-2-

ylmethyl)phenyl]butanoyl]morpholine, and

N-[4-[3-(5,6-dimethoxy-3-methyl-1,4-benzoquinon-2-ylmethyl)phenyl]butanoyl]isopropylamine.

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16. (Thrice Amended) The method according to claim 40 wherein R_1 and R_2 are a hydrogen atom, a methyl group, or a methoxy group.

hydrogen atom or a methyl group.

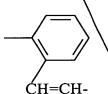
(Thrice Amended) The method according to claim 40 wherein R₃ is a

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(Thrice Amended) The method according to claim 40 wherein Z is

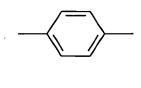


and n is an integer 0.

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20. (Thrice Amended) The method according to claim 40 wherein Z is

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and n is an integer 1, 2, or 3.

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COOR₅ wherein R_5 is a hydrogen atom, an optionally substituted alkyl group having 1 to 8 carbons, an optionally substituted phenyl group, or an optionally substituted aralkyl group having 7 to 11 carbons.

V V

CONR₆R₇ wherein R₆ and R₇ are each independently a hydrogen atom, an optionally substituted alkyl group having 1 to 8 carbons, an optionally substituted bicyclic unsaturated

131

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or partially saturated hydrocarbon ring group having 9 to 11 carbons, an optionally substituted heterocyclic group, an optionally substituted phenyl group, an optionally substituted aralkyl group having 7 to 11 carbons, or a heteroaryl- C_1 - C_3 -alkyl group, or R_6 and R_7 , together with the nitrogen atom to which they are attached, represent a heterocyclic group which may further contain a nitrogen, oxygen, and/or sulfur atom.

(Thrice Amended) The method according to claim 40 wherein R_4 is a group $-\text{CONR}_6R_7$ wherein R_6 and R_7 , together with the nitrogen atom to which they are attached, represent a 5- to 10-membered optionally substituted, nitrogen-containing heterocyclic group which may contain, in addition to the carbon and nitrogen atom, 1 to 3 heteroatoms selected from the group consisting of a nitrogen, oxygen and sulfur atom, the carbon atom on said cyclic group being optionally a ketone form or the sulfur atom on said cyclic group being optionally an oxide form.

73 A_4 . (Thrice Amended) The method according to claim 46 wherein R_1 and R_2 are a methyl group or a methoxy group; R_3 is a methyl group: R_4 is a carboxyl group which is optionally esterified or amidated; Z is

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and n is an integer 1, 2, or 3.

Application No. 09/424,059 Attorney's Docket No. 001560-376 Page 21

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Thrice Amended) The method according to claim 40 wherein the suppressing agent for the gene expression of one or more substances is selected from the group consisting of IL-1 TNF-α, IL-2, IL-6, IL-8, iNOS, granulocyte colony-stimulating factor, inteferon-β, ICAM-1, VCAM-1, ELAM-1, plasminogen activator-inhibiting factor I, major histocompatibility system class I, major histocompatibility system class II, β2-microglobulin, immunoglobulin light chain, serum amyloid A, angiotensinogen, complement B, complement C4, c-myc, HIV, HTLV-1, SV40, CMV, and adenovirus.

- 26. (Thrice Amended) The method according to claim 40 which is a prophylactic or treatment for inflammatory diseases.
- 27. (Thrice Amended) The method according to claim 40 which is a prophylactic or treatment for autoimmune diseases.
- 28. (Thrice Amended) The method according to claim 40 which is a prophylactic or treatment for viral diseases.

38. (Amended) A method for inhibiting NF-κB comprising administering to a patient in need of NF-κB inhibition a benzoquinone derivative represented by the following general formula (1):

5.6 C)

133

Page 22

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$$\begin{array}{c|c}
 & O \\
 & R_1 \\
\hline
 & R_2 \\
\hline
 & CH_2 \\
\hline
 &$$

wherein

Sub

 R_1 , R_2 and R_3 are each independently a hydrogen atom, an alkyl group having 1 to 5 carbons, or an alkoxy group having 1 to 5 carbons;

R₄ is a hydrogen atom, a hydroxymethyl group, an alkyl group, or a carboxyl group which is optionally esterified or amidated;

Z is

CH=CH-CH-CH-CH=CH-

and, n is an integer from 0 to 6, or its hydroquinone form, or a pharmaceutically acceptable salt thereof.

Page 23

39. (Amended) A method for preventing or treating diseases caused by the activation of NF-κB comprising administering to a patient a benzoquinone derivative represented by the following general formula (1):

S M

$$R_1$$
 R_2
 CH_2
 Z
 CH_2
 R_3

wherein

 R_1 , R_2 , and R_3 are each independently a hydrogen atom, an alkyl group having 1 to 5 carbons, or an alkoxy group having 1 to 5 carbons;

R₄ is a hydrogen atom, a hydroxymethyl group, an alkyl group, or a carboxyl group which is optionally esterified or amidated;

Z is

Application No. <u>09/424,059</u> Attorney's Docket No. <u>001560-376</u> Page 24

CH=CH-

and, n is an integer from 0 to 6,

or its hydroquinone form, or a pharmaceutically acceptable salt thereof.

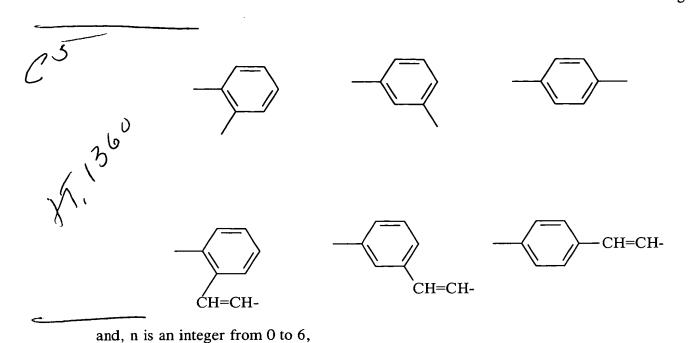
(Amended) A method for inhibiting TNF- α production comprising administering to a patient in need of TNF- α inhibition a benzoquinone derivative represented by the following general formula (1):

 $\begin{array}{c} \begin{array}{c} \begin{array}{c} \\ \\ \\ \\ \\ \end{array} \end{array}$

wherein R_1 , R_2 and R_3 are each independently a hydrogen atom, an alkyl group having 1 to 5 carbons, or an alkoxy group having 1 to 5 carbons,

R₄ is a hydrogen atom, a hydroxymethyl group, an alkyl group, or a carboxyl group which is optionally esterified or amidated;

Z is



or its hydroquinone form, or a pharmaceutically acceptable salt thereof.

41. (Amended) A method for preventing or treating diseases caused by the excessive production of TNF-a comprising administering to a patient a benzoquinone derivative represented by the following general formula (1):

$$R_1$$
 R_2
 CH_2
 Z
 CH_2
 R_3

wherein R_1 , R_2 and R_3 are each independently a hydrogen atom, an alkyl group having 1 to 5 carbons, or an alkoxy group having 1 to 5 carbons;

Application No. <u>09/424,059</u> Attorney's Docket No. <u>001560-376</u> Page 26

 R_4 is a hydrogen atom, a hydroxymethyl group, an alkyl group, or a carboxyl group which is optionally esterified or amidated;

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REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. §1.112, are respectfully requested.

The Applicant has canceled or amended all composition of matter claims or compound claims. All of the claims of record are now directed to methods of use. The two separate methods of use are directed to the inhibition of NF- κ B or the inhibition of TNF- α production. A further discussion of the amendments will be set forth below.

